UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/991,628	11/05/1997	JACK L. STOMINGER	HUIP-P02-001	2823

28120 7590 08/23/2006

FISH & NEAVE IP GROUP
ROPES & GRAY LLP
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/991,628	STOMINGER ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,35,40 and 43-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32, 35, 40 and 43-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/5/06 has been entered.

2. Applicant's amendment filed 6/5/06 is acknowledged, and has been entered.

Claims 32, 35, 40 and 43-46 are pending and are presently being acted upon.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 32 and 43-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed inventions.

The instant claims encompass: a composition comprising a pharmaceutically acceptable carrier and an isolated polypeptide consisting of an amino acid sequence, wherein said amino acid sequence defines a sequence motif containing core MHC binding residues *comprising* a motif recited in instant claims 32, 44, 45 or 46, said motif based upon the structure of the binding pocket of a DRβ1*0402 protein that is associated with PV (claims 32 and 43), or of a DRβ1*1501 protein that is associated with MS (claims 44-46), wherein said polypeptide is a non-myelin basic protein polypeptide, and wherein the said polypeptide *does not bind* either a DRβ1*0402 protein that is associated with PV, nor a DRβ1*1501 protein that is associated with MS and may not stimulate a T cell, *and is of unlimited length* (claims 32 and 44-46) or is 15 amino acid residues in length (claim 43), and that does not have to be a subsequence of any protein,

including one that is an autoantigen associated with PV or MS, and wherein the polypeptide may possess partial structure in having some or all anchor residues for binding to the recited DR allele.

The polypeptide recited in instant claim 32 is of undisclosed partial structure that comprises the PV #1 motif for P1, P4 and P6 anchor residues for peptide binding to HLA-DRβ1*0402. The polypeptide recited in instant claims 44-46 is also of undisclosed partial structure that comprises one of the MS #1-#3 motifs with the P1 and P4 anchor residues and the P-1, P2, P3 and P5 TCR contact residues for binding to HLA-DRβ1*1501.

The specification on page 52 at lines 25-27 discloses that the term "core MHC binding residues" means the residues of an epitope corresponding to the P-1 to P-9 positions of a peptide bound to an HLA-DR molecule. The specification further discloses that there are *5 binding pockets in MHC* (class II, DR), P1, P4, P6, P7 and P9 (page 19 at lines 17-25), at least two of which (page 19 at lines 29-31, page 20, lines 5-6) are used via consideration of the chemical nature and size of said binding pockets (page 20 at lines 9-23) for determination of the sequence motif of the corresponding peptide that binds to the MHC molecule (page 19 at lines 29-31). The specification discloses that HLA-DR4 (DRβ1*0402) or a rare HLA-DQ1 (DQβ1*05032) allele (page 2) are associated with the autoimmune disease pemphigus vulgaris (PV), and that HLA-DRβ1*1501, *i.e.,* HLA-DR2, or DQ1 are associated with MS disease susceptibility (page 2).

Evidentiary reference Rammensee *et al* (MHC Ligands and Peptide Motifs, 1997, pages 200, 204-205 and 227, of record) teach that the P4 anchors for HLA-DRβ1*0402 include Y, F, W, I, L, M, R and N in contrast to Applicant's disclosure that predicts in addition to R, K at P4, but not Y, F, W, I, L, M and N. Rammensee *et al* further teach that although peptide motifs proved extremely helpful in the identification of MHC class I restricted T cell epitopes, for the description of new class II-restricted epitopes, however, conventional epitope mapping still represents the state of the art. Rammensee *et al* teach this is mainly because of the highly degenerate anchor positions in MHC class II presented peptides. Rammensee *et al* teach combining other strategies that value the role of every amino acid residue, not just anchor residues, in the interaction with the MHC class II binding cleft (especially page 227 at Prediction of MHC II Restricted Epitopes section).

Evidentiary reference Reche *et al* (Immunogenetics 2004, 56: 405-419, of record) teach that although anticipation of T cell epitopes is heavily predicated on the prediction of peptide MHC binding, yet prior to MHC binding, correct peptide processing must occur to liberate a peptide from its protein source (first sentence of first full paragraph at column 1 on page 406), and the complexity of such processing makes identification of any pattern related with processing of class II restricted peptides difficult. Reche *et al* teach that cleavage site prediction methods are important adjuncts for T-cell epitope discovery (abstract). Reche *et al* teach that conserved regions flanking the core CD4 T cell epitopes (*i.e.,* class II binding epitopes) may contribute to immunogenicity, said regions being related to antigen processing rather than peptide/MHC interaction (last paragraph of article).

Evidentiary reference O'Sullivan (Applicant's IDS reference) teaches that the presence of putative binding motif residues does not necessarily correlate with actual binding to an MHC molecule because both binders and non-binders may have the putative motif.

The art recognizes that in order to be used for generating an immunogenic or tolerogenic response that said peptide must bind MHC and also present an epitope recognized by T cells. The art recognizes that the T cell epitope differs from the amino acids pertinent to MHC binding.

Evidentiary reference Karin *et al* (J. Exp. Med. 1994, 180: 2227-2237, of record) teaches that a single substitution in an amino acid residue, wherein said amino acid residue plays no role in MHC binding, can completely abrogate the immunogenicity of an otherwise immunogenic peptide (especially summary and Table 1). Thus Karen *et al* establish that amino acid residues not recited in the claimed "human" or "human pathogen" polypeptides, *i.e.,* TCR contact residues, will play a pivotal role in determining whether the peptides recited in the claims are capable of stimulating a T cell.

There is no written description in the specification of the amino acids that constitute the T cell epitope in the peptide possessing the PV motif #1. With the exception of the specific peptides identified by amino acid sequence in the specification such as SEQ ID NO: 1-7 from the contiguous sequence of the PV autoantigen protein desmoglein 3, the skilled artisan cannot envision the detailed structure of the encompassed peptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. In the instant application, the amino acid itself or isolated peptide is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016.

In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (*i.e.,* nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA." See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

Applicant's arguments in the amendment filed 6/5/06 have been fully considered but are not persuasive.

Applicant's position in the said amendment beginning on pages 5-6 under the section entitled "Claim rejections under 35 U.S.C. 112, first paragraph-Written Description" is of record. Briefly, this is: that the claims have been amended such that they do not recite the term "human," such that they do not recite that the polypeptide must bind the TCR and tolerize against an autoantigen of PV or MS, such that they do not recite the intended use "for tolerization," that the claim amendment included changing "an amino acid sequence" to "the amino acid sequence," and including the recitation of DRβ1*01501 or DRβ1*0402.

It is the Examiner's position that: Applicant has overcome some of the issues enunciated in the prior rejection of record by the said claim amendments. However, the instant claims recite a composition comprising a polypeptide that comprises a peptide of partially defined structure and with undisclosed areas within the HLA binding and TCR binding portion of the peptide (claims 32 and 43-46), as well as undisclosed N and C terminal flanking sequences of undisclosed length (claims 32 and 44-46), *i.e.,* the peptides have partial structure, with no recitation of a functional property such as binding to the recited HLA molecule and stimulating a T cell.

It is the Examiner's further position that the number of potential polypeptide species is very large due to the number of proteins that contain an undisclosed number of subsequences possessing a motif for binding to DRβ1*01501 or DRβ1*0402, constituting several million subsequences that would potentially possess the binding motif (see analysis in the prior Office Action of record). If the polypeptides possessing the motif are not subsequences of proteins, then the number of potential polypeptides that could possess the motif is potentially unlimited, as the TCR contact amino acid residues are not specified in the PV#1 motif and the claimed polypeptides contain undisclosed N and C terminal flanking sequences. In addition, evidentiary reference Reche *et al* teach that conserved regions flanking the core CD4 T cell epitopes (*i.e.,* class II binding epitopes) may contribute to immunogenicity, adding to the number of potential peptides.

5. Claims 32 and 43-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a polypeptide consisting of one of SEQ ID NO: 1-7, does not reasonably provide enablement for the claimed pharmaceutical preparation comprising a composition comprising a pharmaceutically acceptable carrier and an isolated polypeptide consisting of an amino acid sequence, wherein said amino acid sequence defines a sequence motif containing core MHC binding residues *comprising* a motif recited in instant claims 32, 44, 45 or 46, i.e., having undisclosed structure and/or unlimited length, said motif based upon the structure of the binding pocket of a DRβ1*0402 protein that is associated with PV (claims 32 and 43), or of a DRβ1*1501 protein that is associated with MS (claims 44-46), wherein said polypeptide is a non-myelin basic protein polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass: The instant claims encompass: a composition comprising a pharmaceutically acceptable carrier and an isolated polypeptide consisting of an amino acid sequence, wherein said amino acid sequence defines a sequence motif containing core MHC binding residues *comprising* a motif recited in instant claims 32, 44, 45 or 46, said motif based upon the structure of the binding pocket of a DRβ1*0402 protein that is associated with PV (claims 32 and 43), or of a DRβ1*1501 protein that is associated with MS (claims 44-46), wherein said polypeptide is a non-myelin basic protein polypeptide, and wherein the said polypeptide *does not bind* either a DRβ1*0402 protein that is associated with PV, nor a DRβ1*1501 protein that is associated with MS and may not stimulate a T cell, *and is of unlimited length* (claims 32 and 44-46) or is 15 amino acid residues in length (claim 43), and that does not have to be a subsequence of any protein, including one that is an autoantigen associated with PV or MS, and wherein the polypeptide may possess partial structure in having some or all anchor residues for binding to the recited DR allele.

The polypeptide recited in instant claim 32 is of undisclosed partial structure that comprises the PV #1 motif for P1, P4 and P6 anchor residues for peptide binding to HLA-DRβ1*0402, and contains undisclosed N and C terminal flanking sequences. The polypeptide recited in instant claims 44-46 is also of undisclosed partial structure that comprises one of the MS #1-#3 motifs with the P1 and P4 anchor residues and the P-1, P2, P3 and P5 TCR contact residues for binding to HLA-DRβ1*1501, and contains undisclosed N and C terminal flanking sequences.

The specification on page 52 at lines 25-27 discloses that the term "core MHC binding residues" means the residues of an epitope corresponding to the P-1 to P-9 positions of a peptide bound to an HLA-DR molecule. The specification further discloses that there are *5 binding pockets in MHC* (class II, DR), P1, P4, P6, P7 and P9 (page 19 at lines 17-25), at least two of which (page 19 at lines 29-31, page 20, lines 5-6) are used via consideration of the chemical nature and size of said binding pockets (page 20 at lines 9-23) for determination of the sequence motif of the corresponding peptide that binds to the MHC molecule (page 19 at lines 29-31). The specification discloses that HLA-DR4 (DRβ1*0402) or a rare HLA-DQ1 (DQβ1*05032) allele (page 2) are associated with the autoimmune disease pemphigus vulgaris (PV), and that HLA-DRβ1*1501, *i.e.,* HLA-DR2, or DQ1 are associated with MS disease susceptibility (page 2).

Evidentiary reference Rammensee *et al* (MHC Ligands and Peptide Motifs, 1997, pages 200, 204-205 and 227, of record) teach that the P4 anchors for HLA-DRβ1*0402 include Y, F, W, I, L, M, R and N in contrast to Applicant's disclosure that predicts in addition to R, K at P4, but not Y, F, W, I, L, M and N. Rammensee *et al* further teach that although peptide motifs proved extremely helpful in the identification of MHC class I restricted T cell epitopes, for the description of new class II-restricted epitopes, however, conventional epitope mapping still represents the state of the art. Rammensee *et al* teach this is mainly because of the highly degenerate anchor positions in MHC class II presented peptides. Rammensee *et al* teach combining other strategies that value the role of every amino acid residue, not just anchor residues, in the interaction with the MHC class II binding cleft (especially page 227 at Prediction of MHC II Restricted Epitopes section).

Evidentiary reference Reche *et al* (Immunogenetics 2004, 56: 405-419, of record) teach that although anticipation of T cell epitopes is heavily predicated on the prediction of peptide MHC binding, yet prior to MHC binding, correct peptide processing must occur to liberate a peptide from its protein source (first sentence of first full paragraph at column 1 on page 406), and the complexity of such processing makes identification of any pattern related with processing of class II restricted peptides difficult. Reche *et al* teach that cleavage site prediction methods are important adjuncts for T-cell epitope discovery (abstract). Reche *et al* teach that conserved regions flanking the core CD4 T cell epitopes (*i.e.,* class II binding epitopes) may contribute to immunogenicity, said regions being related to antigen processing rather than peptide/MHC interaction (last paragraph of article).

Evidentiary reference O'Sullivan (Applicant's IDS reference) teaches that the presence of putative binding motif residues does not necessarily correlate with actual binding to an MHC molecule because both binders and non-binders may have the putative motif.

The art recognizes that in order to be used for generating an immunogenic or tolerogenic response that said peptide must bind MHC and also present an epitope recognized by T cells. The art recognizes that the T cell epitope differs from the amino acids pertinent to MHC binding.

Evidentiary reference Karin *et al* (J. Exp. Med. 1994, 180: 2227-2237, of record) teaches that a single substitution in an amino acid residue, wherein said amino acid residue plays no role in MHC binding, can completely abrogate the immunogenicity of an otherwise immunogenic peptide (especially summary and Table 1). Thus Karen *et al* establish that amino acid residues not recited in the claimed "human" or "human pathogen" polypeptides, *i.e.,* TCR contact residues, will play a pivotal role in determining whether the peptides recited in the claims are capable of stimulating a T cell.

There is no guidance in the specification how to make and/or use and as to what alterations result in a functional polypeptide comprising a partial motif for binding to HLA-DRβ1*0402 or DRβ1*1501 and that contains undisclosed N and C terminal flanking sequences, *i.e.,* one that binds to a subtype of the recited HLA-DR *and* to a TCR *and* is capable of stimulating a T cell. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions/additions would be acceptable to retain functional activity, *i.e.,* bind to any number of undisclosed HLA-DR molecules, bind to a T cell and cause stimulation or tolerization, it would require undue experimentation for one of skill in the art to arrive at amino acid sequences that would have functional activity. In other words, since it would require undue experimentation to identify amino acid sequences that have functional activity, it would require undue experimentation to make and/or use the corresponding sequences. The enablement provided by the specification is not commensurate with the scope of the claims.

Applicant's arguments in the amendment filed 6/5/06 have been fully considered but are not persuasive.

Applicant's position in the said amendment beginning on page 6 and continuing through page 8 is of record in Applicant's said amendment, briefly that: (1) that the claims have been amended such that they do not recite the term "human," such that they do not recite that the polypeptide must bind the TCR and tolerize against an autoantigen of PV or MS, such that they do not recite the intended use "for tolerization," that the claim amendment included changing "an amino acid sequence" to "the amino acid sequence," and including the recitation of DRβ1*01501 or DRβ1*0402, (2) the specification discloses that the peptides may be used for *in vitro* assays that aid in the diagnosis and classification of PV and MS, in screening of T cells from a subject against a battery of peptides of the invention, where the more peptides the T cells react to, the greater the likelihood that the subject is predisposed to an autoantigenic response, and (3) when the TCR contacting residues of a pathogen are known, they can be incorporated into the peptides of the invention to generate a vaccine.

It is the Examiner's position that: Applicant has overcome some of the issues enunciated in the prior rejection of record by the said claim amendments. However, the instant claims recite a polypeptide that comprises a peptide of partially defined structure and with undisclosed areas within the HLA binding and TCR binding portion of the peptide (claims 32 and 43-46), as well as undisclosed N and C terminal flanking sequences of undisclosed length (claims 32 and 44-46), *i.e.,* have partial structure, with no recitation of a functional property such as binding to the recited HLA molecule and stimulating a T cell.

It is the Examiner's further position that the number of potential polypeptide species is very large due to the number of proteins that contain an undisclosed number of subsequences possessing a motif for binding to DRβ1*01501 or DRβ1*0402, constituting several million subsequences that would potentially possess the binding motif (see analysis in the prior Office Action of record). If the polypeptides possessing the motif are not subsequences of proteins, then the number of potential polypeptides that could possess the motif is potentially unlimited, as the TCR contact amino acid residues are not specified in the PV#1 motif and the claimed polypeptides contain undisclosed N and C terminal flanking sequences. In addition, evidentiary reference Reche *et al* teach that conserved regions flanking the core CD4 T cell epitopes (*i.e.,* class II binding epitopes) may contribute to immunogenicity, adding to the number of potential peptides.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 32, 35, 40 and 43-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32 and 44-46 are indefinite in the recitation of "is based upon the structure of the binding pocket of" a(n) DRβ1*0402 or an DRβ1*1501 protein because it is not clear what is meant, *i.e.,* what the metes and bounds of the said claims are.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 32, 35, 40 and 43-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3 and 4 of U.S. Patent No. 5,874,531 (of record). Although the conflicting claims are not identical, they are not patentably distinct from each other because the peptide or composition comprising the peptides of claims 1 and 3 of the '531 patent are encompassed by the instant claims 32, 35, 40 and 43, *i.e.,* SEQ ID NO: 1-7 have the motif recited in instant claim 32, and the peptide or composition comprising the peptide of claims 2 and 4 of the '531 patent are encompassed by the instant claims 44-46, *i.e,* SEQ ID NO: 8 has the MS #18-20 motifs, SEQ ID NO: 11 has the MS #19-20 motifs, SEQ ID NO: 12-15 have the MS #19 motif, and SEQ ID NO: 13 has the MS #20 motif.

The Examiner notes Applicant's remarks on page 8 in Applicant's amendment filed 6/5/06, *i.e.,* that Applicant will submit a terminal disclaimer, if necessary, upon indication of allowable subject matter; however, the Examiner may not hold this rejection in abeyance.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section

351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claim 46 is rejected under 35 U.S.C. 102(a) as being anticipated by WO 94/020127 A1.

WO 94/020127 A1 teaches pharmaceutical compositions comprising peptides of the invention (page 23 at lines 32-38 and page 24 at lines 1-15) such as human PLP peptide 158 (Appendix II on pages 118 and 126) and a pharmaceutically acceptable carrier such as 0.8% saline (page 24 at lines 2-3). The human PLP peptide 158 comprises the MS #20 motif (bolded and underlined), *i.e.,* ALTV**VWLL**VFA.

With regard to the limitation "is based upon the structure of the binding pocket of an HLA-DRβ1*1501 protein that is associated with multiple sclerosis," the claimed peptide composition appears to be the same as the peptide composition of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the peptide composition of the art and the peptide composition of the instant claim.

12. Claims 44-46 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,329,499 B1.

During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification." Applicant always has the opportunity to amend the claims during prosecution and broad interpretation by the Examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. *In re Prater*, 162 USPQ 541, 550 - 51 (CCPA 1969).

The instant specification does not disclose the definition of "a non-myelin basic protein polypeptide," which opens the claim to read upon prior art that teaches myelin basic protein analog peptide compositions.

U.S. Patent No. 6,329,499 B1 discloses pharmaceutical compositions comprising a peptide analog of human MBP amino acid residues 86-99 (the native peptide being SEQ ID NO: 3 of the art reference), such as the peptide analog wherein position 91 is altered from K to R (claim 7), *i.e.,* PVVHFF**R**NIVTPRTP, or such as peptides having substitutions outside of amino acid residues 86-90 (claim 8), and further comprising a pharmaceutically acceptable carrier such as PBS (column 9 at lines 64-67 and column 10 at lines 1-35). The K91R analog peptide comprises

MS motif #18, #19 and #20 of the instant claims, *i.e.,* VVHFFR (MS #19), VHFFR (MS #19) and VHFF (MS #20).

With regard to the limitation "wherein said polypeptide is a non-myelin basic protein polypeptide, the analog peptide is no longer a myelin basic protein polypeptide since it's sequence has been altered.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 44 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Registry Accession No. 160218-02-0 (18 January 1992) in view of De Bruijin *et al* (Eur. J. Immunol. 1991, 27: 2963-2970, of record).

Registry Accession No. 160218-02-0 teaches a peptide consisting of the sequence VVHFFKDI, wherein said peptide comprises the MS #18 and MS #20 motifs of instant claims 44 and 46, *i.e.,* VVHFFK and VHFF, respectively.

Registry Accession No. 160218-02-0 does not teach the said peptide in a composition comprising a pharmaceutically acceptable carrier.

De Bruijin *et al* teach formulating peptides in PBS in order to store them.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have formulated the peptide taught by Registry Accession No. 160218-02-0 in the PBS taught by De Bruijin *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to dissolve the peptide in a carrier that is compatible with storing the said peptide as taught by De Bruijin *et al.*

With regard to the limitation "is based upon the structure of the binding pocket of an HLA-DRβ1*1501 protein that is associated with multiple sclerosis," the claimed peptide composition appears to be similar to the peptide composition of the prior art absent a showing of unobvious differences. With regard to the limitation "wherein said polypeptide is a non-myelin basic protein polypeptide, the peptide appears to be similar to the peptide composition of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction

between the peptide composition of the art and the peptide composition of the instant claim.

15. Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Registry Accession No. 155029-62-2 (13 May 1994) in view of De Bruijin *et al* (Eur. J. Immunol. 1991, 27: 2963-2970, of record).

Registry Accession No. 155029-62-2 teaches a peptide consisting of the sequence VVHFFKDI, wherein said peptide comprises the MS #20 motif of instant claim 46, *i.e.*, VHFF.

Registry Accession No. 155029-62-2 does not teach the said peptide in a composition comprising a pharmaceutically acceptable carrier.

De Bruijin *et al* teach formulating peptides in PBS in order to store them.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have formulated the peptide taught by Registry Accession No. 155029-62-2 in the PBS taught by De Bruijin *et al*.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to dissolve the peptide in a carrier that is compatible with storing the said peptide as taught by De Bruijin *et al*.

With regard to the limitation "is based upon the structure of the binding pocket of an HLA-DRβ1*1501 protein that is associated with multiple sclerosis," the claimed peptide composition appears to be similar to the peptide composition of the prior art absent a showing of unobvious differences. With regard to the limitation "wherein said polypeptide is a non-myelin basic protein polypeptide, the peptide appears to be similar to the peptide composition of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the peptide composition of the art and the peptide composition of the instant claim.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
August 18, 2006

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600